

REMARKS

I. Claim Amendments

By the foregoing amendments to the claims, claims 20, 24, 36, and 39 have been amended, and claims 22, 23, 29, and 35 have been canceled. In particular, the claims have been amended to recite that the histone deacetylase inhibitor “is administered before administration of the adeno-associated virus vector.” This amendment is supported at least at page 15, first paragraph; and at the sentence spanning pages 15 and 16 of the specification as filed.

The amendments to the claims, including cancellation of claims, have been made without prejudice or disclaimer to any subject matter recited or canceled herein. Applicants reserve the right to file one or more continuation and/or divisional applications directed to any canceled subject matter. No new matter has been added, and entry of the foregoing amendments to the claims is respectfully requested.

III. Response to Claim Rejections Under 35 U.S.C. § 102

Claims 20, 22, 24, 27, 29, 30, 36, 37 have been rejected under 35 U.S.C. § 102(b), as allegedly being anticipated by Townes et al., WO Publication No. 97/47307. This rejection is respectfully traversed.

Not to acquiesce to the rejection, but to advance prosecution, as noted above the claims have been amended to recite that the histone deacetylase inhibitor is administered before administration of the adeno-associated virus vector. Townes et al. does not teach administering the histone deacetylase inhibitor before administration of the adeno-associated virus vector. For at least this reason, the present claims are not anticipated by Townes et al. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

IV. Response to Claim Rejections Under 35 U.S.C. § 103

Claims 20-39 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Townes et al. in view of Nakajima et al., Exp Cell Res 241:126-133 (1998), and Alisky et al., Hum Gene Ther 11:2315-2329 (2000). This rejection is respectfully traversed.

The present inventors have discovered that histone deacetylase inhibitors can enhance gene expression of an episomal AAV genome which has not undergone chromosomal integration. Thus, the inhibitor can be administered before administration of an AAV vector.

In contrast to the present invention, Townes et al. teaches that induced foreign genes exist in cells over a long period and then a small population of them are chromosomally integrated in cells (i.e. not episomal). The percentage of chromosomal integration of AAV vector genomes in cells is believed to be extremely low. The experiments in Townes et al. use only such rarely seen cells which had undergone transduction with a foreign gene after long-term incubation. These cells were selected by screening with a drug resistance marker gene and amplified. Thus, in the reference examples, the transgenes that were tested had become a part of the cell chromosomes due to long-term incubation, and had also undergone histone modification and silencing along with the cell chromosomes. The examples therefore tested the reactivation of the expression of the silenced transduced genes. Because AAV vector gene expression primarily derives from episomal AAV vector genomes, which are not integrated into cellular chromosomes, Townes et al. relates to a completely different system than the typical AAV vector mediated transgene expression pattern in cells which is the focus of the present application.

Thus, taken as a whole, in contrast to the present claims Townes et al. teaches treating a patient with histone deacetylase inhibitors after gene therapy has been completed. In light of this reference, a person of ordinary skill in the art would not have been motivated to administer the inhibitor before vector administration, and would not have reasonably predicted that the present methods would be successful. Accordingly, the present claims are not obvious over Townes et al. Furthermore, the additional references cited by the Examiner do not remedy the serious deficiencies of Townes et al.

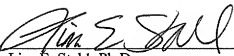
In view of the above, Applicants respectfully request reconsideration and withdrawal of this rejection.

CONCLUSION

In view of the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.

In the event that there are any questions related to this response, or the application in general, it would be appreciated if the Examiner would telephone the undersigned attorney at the below-listed telephone number concerning such questions so that prosecution of this application may be expedited.

Respectfully submitted,

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